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lesson of the month (1)

Rifaximin may have a dramatic effect on hepatic encephalopathy

With a steadily increasing healthcare burden, all physicians must be aware of methods to manage the complications of chronic liver disease, including hepatic encephalopathy. Approved by the Food and Drug Administration in the USA and several European countries as a treatment for recurrent hepatic encephalopathy an increasing number of patients are now receiving rifaximin for this condition. This 'lesson of the month' highlights the dramatic effect that rifaximin may have on hepatic encephalopathy.

Lesson

A 75-year-old man with an established diagnosis of liver cirrhosis secondary to non-alcoholic steato-hepatitis underwent primary endoscopic variceal ligation (EVL) for grade 3 oesophageal varices after having been intolerant of propranolol as primary prophylaxis against variceal haemorrhage. He had a background history of type 2 diabetes mellitus, rheumatoid arthritis and atrial fibrillation. Eight days after EVL he suffered a profuse gastrointestinal bleed secondary to a ligation ulcer. The bleeding continued despite repeated endotherapy, terlipressin and the use of a Sengstaken Blakemore tube, thus necessitating insertion of a transjugular intrahepatic portosystemic shunt (TIPSS) that resulted in complete haemostasis. Until this admission the patient had been a keen artist (Fig 1).

One year later, the patient had enrolled in a postgraduate master of literature degree at university; however, he expressed frustration at loss of balance and intermittent confusion that was interfering with his studies. A clinical diagnosis of hepatic encephalopathy was confirmed by high levels of ammonia in serum on serial testing in the outpatient clinic. Hepatic encephalopathy is a recognised complication of TIPSS, occurring in as many as 45% of patients and more commonly in older patients and those with renal impairment, hyponatraemia and hypoalbuminaemia.[1] The patient started lactulose as treatment for hepatic encephalopathy, but this did not produce any significant improvement. Over time, the patient's level of function deteriorated to the point where he could no longer study or paint and struggled even with handwriting (Fig 2).

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Fig 1. Example of patient's artwork prior to transjugular intrahepatic portosystemic shunt (TIPSS).

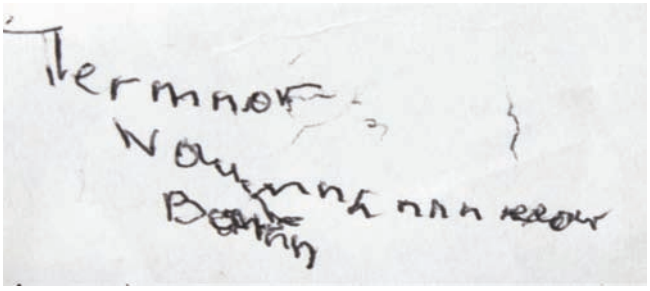

Fig 2. Example of patient's handwriting during a period of hepatic encephalopathy.

Subsequently, rifaximin was added to his prescription with dramatic improvement. He returned to his university studies and graduated successfully at the age of 75 years. Figure 3 shows examples of his handwriting and artwork after rifaximin was introduced.

Discussion

Rifaximin has recently been identified as a safe, efficacious and cost-effective treatment for hepatic encephalopathy. It is a rifamycin-derived oral antibiotic that is more commonly associated with treatment of travellers' diarrhoea. As rifaximin has almost no absorption from the gastrointestinal tract and does not induce cytochrome P450 enzymes, it is well tolerated, with few drug interactions or side effects.[2] Importantly, rifaximin can be used safely in patients with liver disease to reduce production of ammonia by bacteria in the gut.

In patients with acute hepatic encephalopathy, rifaximin has shown comparable efficacy to lactulose.[3] Bucci *et al* found that

Fig 3. Examples of patient artwork (a) and handwriting (b) after initiation of treatment with rifaximin.

rifaximin was better tolerated than lactulose, with a limited number of side effects compared with the symptoms of diarrhoea, flatulence and dyspepsia experienced by about half of patients taking lactulose. In addition, patients' mental state seemed to respond faster in those receiving rifaximin than in those taking lactulose.

Rifaximin also seems to reduce the need for hospitalisation due to hepatic encephalopathy. An American study showed that although the monthly drug cost of rifaximin was higher than that for lactulose ($620 per month vs $50 per month), those receiving rifaximin required fewer hospitalisations over an observation period of one year and those who were admitted had a shorter average length of stay.[4] Consequently, the total cost of therapy per patient per year was lower with rifaximin than with lactulose ($7,958 vs $13,285).

A further recent study in patients with recurrent hepatic encephalopathy in remission looked at the six-month incidence of breakthrough symptoms.[5] These were noted in 22.1% of patients treated with rifaximin compared with 45.9% of those receiving placebo. More than 90% of patients in both arms received lactulose, which confirms that the addition of rifaximin may be very useful to control hepatic encephalopathy when monotherapy with lactulose is insufficient.

This lesson highlights pictorially the profound effect that this drug can have on the level of function of patients who experience hepatic encephalopathy. Clinicians should be aware of rifaximin as an additional or alternative agent to lactulose in the treatment of this condition.

References

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